Annals of Clinical and Analytical Medicine
Original Research

Are shock index, modified shock index, NLR and qSOFA useful in making COVID-19 intensive care follow-up decisions?

Markers of COVID-19 intensive care follow-up decisions

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Abstract
Aim: To meet the increasing intensive care and mechanical ventilator needs during the COVID-19 pandemic process, parameters that will enable rapid assessment and decision-making at the bedside are required in emergency services. The aim is to provide rational use of intensive care units by determining appropriate parameters that can be used to evaluate the intensive care follow-up indication.
Material and Methods: Demographic data,vital signs, and hemogram results were recorded during the consultation in terms of intensive care follow-up requirements of the patients. The qSOFA, shock index, modified shock index, and the neutrophil-lymphocyte ratio were calculated.
Results: Three hundred patients were included in the study.The median age was 69.2 years, 88% of the patients had at least one comorbid disease. The neutrophil-lymphocyte ratio was significant in predicting the need for intubation, but is not an independent risk factor. Male gender, qSOFA scores and need for intubation were predictors of intensive care mortality.
Discussion: We found out that no scoring system can predict the requirement of intubation, but qSOFA is effective in showing mortality when making intensive care follow-up decisions for COVID-19 patients consulted in emergency departments.

Keywords
Coronavirus, Intensive Care Units, Modified Shock Index, Neutrophil-to-Lymphocyte Ratio, QSOFA, Shock Index

DOI: 10.4328/ACAM.20796 Received: 2021-07-21 Accepted: 2021-10-05 Published Online: 2021-10-09 Printed: 2021-12-01 Ann Clin Anal Med 2021;12(12):1423-1426
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Introduction

Having broken out in Wuhan province of China in December 2019 and being caused by acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), Coronavirus Disease 2019 (COVID-19) rapidly spread around the world and caused a pandemic [1]. In a report of 72.314 cases, 14% of the patients were reported to be severely ill, including dyspnoea, low blood oxygen saturation ≤93%, increased respiratory rate and increased oxygen demand [2]. Moreover, 5% were critically ill accompanied by respiratory failure, septic shock and/or multi-organ dysfunction. As the COVID-19 outbreak spread, the need for intensive care units and the increasing number of patients during the pandemic process necessitated the determination of criteria for identifying patients requiring intensive care follow-up [3]. Since the first patient was diagnosed in our country, algorithms and guidelines aimed at guidance strategies in patient follow-up have been prepared and updated by expert scientific committee members [4]. However, for patients who are treated in the emergency service, there are no definitive criteria to predict cases that will develop a need for intubation or have a critical course in the decision-making process of COVID-19-related intensive care follow-up.

Shock index (SI), modified shock index (MSI), quick sequential organ failure assessment (qSOFA) and neutrophil-lymphocyte ratio (NLR) were the parameters used to diagnose patients in shock [5-8]. In patients suffering from severe COVID-19, the clinical course is acute and aggressive, following a course similar to shock [2]. However, their role in determining critically ill patients with COVID-19 is not clear.

In order to determine the Intensive Care Unit (ICU) follow-up process of COVID-19 patients and to identify patients' invasive mechanical ventilation (IMV) requirement early, parameters are necessary for rapid evaluation. Therefore, in this study, the success rate of the scoring systems was evaluated in patients consulted for an indication of ICU follow-up. Our primary study has focused on identifying appropriate parameters for the early diagnosis of critically ill patients.

Material and Methods

Following the approval of the Institutional Ethics Committee [Protocol number: 2020/514/179/13, date: 11/06/2020], informed consent was obtained from the relatives of all COVID-19 patients who were treated in the intensive care unit between March 23 and September 30, 2020. The data were retrospectively analyzed. The study was carried out in accordance with the ethical principles stated in the guides of "Good Medical Practices" and "Good Clinical Practices" of the Declaration of Helsinki. The primary endpoint of the study was determined as the development of intubation and the need for IMV, and the secondary as the presence of mortality in the ICU.

COVID-19 diagnosis:

Nasal and oral swab samples were taken from the patients who applied to the emergency department with complaints of fever, weakness, cough, shortness of breath, chest or headache, abdominal pain, or diarrhea. The diagnosis of COVID-19 followed a positive Real-Time Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) result.

Data collection:

The demographic data including age, gender, comorbid diseases, number of days of treatment before the ICU admission, chest tomography involvement weight (Mild = less than 50% involvement, Moderate-Severe = more than 50% involvement), tracheal intubation requirement, and ICU mortality were recorded. The examined comorbid diseases were hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), cerebrovascular disease (CVD), chronic obstructive pulmonary disease (COPD), asthma, and malignancy (CA). During the consultation, vital parameters such as respiratory rate (RR), Glasgow Coma Score (GCS), heart rate (HR), systolic (SBP) and diastolic blood pressures (DBP), calculated mean arterial pressure (MAP) and NLR were recorded. SI, MSI, qSOFA, and NLR were calculated and the relationship between these parameters and ICU survival and the need for tracheal intubation were determined. The data of the patients were evaluated according to intubation and mortality and were interpreted under two main tables.

SI was calculated with the formula '' [SpO 2 / FiO 2] / RR '' [5].

MSI was calculated with the formula '' [SpO 2 / FiO 2] / RR '' [6].

The qSOFA score included 3 clinical criteria that assign 1 point for blood pressure (SBP ≤ 100 mmHg), respiratory rate (>22 breaths / minute) and consciousness (GCS score <15). The score ranges from 0 to 3 points. A score of 2 or more was considered positive [7]. The NLR value was calculated using a hemogram test, which is routinely performed during the admission of patients to the emergency department. The study included all adult patients whose necessary data were available and who were consulted with the diagnosis of COVID-19 because of the necessity of follow-up in the ICU.

Statistical analysis:

Statistical analyzes were performed with the SPSS 21 program. Quantitative variables, expressed as mean ± Standard deviation, were compared using the Oneway Anova test. Qualitative variables were expressed as percentages and compared using either the chi-square test or Fisher's exact test. A multivariate analysis was performed to evaluate the significant variables associated with intubation and mortality. A $p < 0.05$ was considered significant.

Results

The data of 300 patients who were followed up in the ICU due to COVID-19 were evaluated. The median age of the patients was 69.2 years, 63.7% of them were males. In 88% of the patients, at least one comorbid disease was present, and the most common accompanying disease was hypertension with a rate of 52.2%. While 66 patients were followed without intubation, 234 patients constituted the intubated group. There was no difference between the groups in terms of age and comorbid diseases, but the male gender ratio was higher in the intubated group . The average number of treatment days the patients received before ICU admission was 1.98 ± 3.1 days, and there was no difference between the two groups according to the tracheal intubation requirement. Computed Tomography (CT) evaluation of 232 patients revealed moderate to severe involvement, and both groups were similar. To determine the need for intubation, no difference was observed between the two groups in terms of qSOFA, SI, and MSI calculated during

admission to ICU. A higher NLR was found in the intubated group (9.4 vs 17.2; p <0.05, Table 1) in univariate analysis, but it is not an independent risk factor for intubation.
Table 2 shows the relationship between patient demographics and mortality. The two groups were similar in terms of age and presence of comorbidity. Male patients had a significantly higher mortality rate (69.7%). No significant difference was observed between the CT classification of the patients and the treatment day before ICU and the presence of mortality (Table3). Table 3 also examines the criteria that can be used to predict mortality during admission of patients to ICU. There was no difference between the two groups in terms of SI and MSI during ICU admission. While 29.9% of patients with mortality were Qsofa-positive, this rate was 17.2% in patients who did not develop, and the difference was statistically significant. While the mean NLR value of 201 patients in the mortality group was 18.1, it was 10.2 in 99 patients who did not die, but it is not an independent risk factor for mortality (p=0,100). Besides, there was a significant correlation between intubation and mortality.

Table 1. Factors affecting the need for intubation

	Intubation - n: 66	Intubation + n: 234	Total n: 300	p value
CT involvement Mild	20 (%30.3)	48 (%20.5)	68 (%22.7)	0.068[b]
Moderate to Severe	46 (%69.7)	186 (%79.5)	232 (%77.3)	
Pre ICU treatment day	2.2±2.8	1.91±3.2	1.98±3.1	0.519[a]
q SOFA (+)	14 (%21.2)	63 (%26.9)	77 (%25.7)	0.220[b]
SI	0.25±0.44	0.32±0.46	0.30±0.46	0.362[a]
MSI	0.69±0.55	0.71±0.53	0.70±0.53	0.868[a]
NLR	9.4±9.3	17.2±25.3	15.5±23.0	0.015[a]
ICU mortality	9 (%13.6)	192 (%82.1)	201 (%67.0)	0.000[b]

[a]One-way Anova, [b]Pearson Chi-Square, CT: Computerized Tomography, ICU: Intensive care units, qSOFA: Quick Sequential Organ Failure Assessment, SI: Shock Index, MSI: Modified Shock Index, NLR: Neutrophil-to-Lymphocyte Ratio

Table 2. The effect of demographic characteristics of the patients on mortality

	Mortality - n: 99	Mortality + n: 201	Total n: 300	p value
Age	68.5±14.4	69.5±13.5	69.23±13.8	0.912[a]
Gender: Female	48 (%48.5)	61 (%51.5)	109 (%36.3)	0.002[b]
Male	51 (%51.5)	140 (%69.7)	191 (%63.7)	
Additional Illness	88 (%88.9)	176 (%87.6)	264 (%88.0)	0.449[b]
HT	55 (%55.6)	99 (%49.3)	154 (%51.3)	0.183[b]
DM	39 (%39.4)	52 (%25.9)	91 (%30.3)	0.012[b]
CVD	1 (%1.0)	7 (%3.5)	8 (%2.7)	0.197[b]
COPD	25 (%25.3)	45 (%22.4)	70 (%23.3)	0.340[b]
Asthma	24 (%24.2)	40 (%19.9)	64 (%21.3)	0.236[b]
CA	17 (%17.2)	51 (%25.4)	68 (%22.7)	0.072[b]
CAD	27 (%37.4)	78 (%38.8)	115 (%38.3)	0.456[b]

[a]One-way Anova, [b]Pearson Chi-Square, HT: Hypertension, DM: Diabetes Mellitus, CVD: Cerebrovascular Disease, COPD: Chronic Obstructive Pulmonary Disease, CA: Malignancy, CAD: Coronary Artery Disease

Table 3. Factors affecting the ICU mortality

	Mortality - n: 99	Mortality + n: 201	Total n: 300	p value
CT involvement Mild	26 (%26.3)	42 (%20.9)	68 (%22.7)	0.184[b]
Moderate to Severe	73 (%73.7)	159 (%79.1)	232 (%77.3)	
Pre ICU treatment day	2.0±2.7	1.95±3.3	1.98±3.1	0.836[a]
q SOFA (+)	17 (%17.2)	60 (%29.9)	77 (%25.7)	0.012[b]
SI	0.25±0.44	0.32±0.47	0.30±0.46	0.180[a]
MSI	0.68±0.54	0.72±0.53	0.70±0.53	0.655[a]
NLR	10.2±9.1	18.1±27.0	15.5±23.0	0.005[a]
Intubation	42 (%42.4)	192 (%95.5)	201 (%67.0)	0.000[b]

[a]Oneway Anova, [b]Pearson Chi-Square, CT: Computerized Tomography, ICU: Intensive care units, qSOFA: Quick Sequential Organ Failure Assessment, SI: Shock Index, MSI: Modified Shock Index, NLR: Neutrophil-to-Lymphocyte Ratio

Discussion

In this study, we investigated the possibility of using SI, MSI, NLR and qSOFA scores to be indicators of mortality . Mortality was higher in cases with a high intubation ratio and positive qSOFA. In our study, male gender and the need for mechanical ventilation were associated with a high mortality rate. Our results were similar with a study conducted in Italy [9]. The mortality rate was higher in patients requiring IMV. However, mortality was not observed in a small group of extubated patients in the intensive care unit. All these patients were discharged to the ward.
Studies have shown that clinical signs of shock are present in critical COVID-19 patients, even in the absence of hypotension [10]. This has revealed the presence of a viral sepsis mechanism in COVID-19. According to the Chinese data, the prevalence of shock reported in adult patients with COVID-19 varies greatly depending on the patient population studied and the definition of shock (1% to 35%) [2]. In another analysis, acute respiratory distress syndrome (ARDS), septic shock, and acute renal failure were identified as possible clinical manifestations associated with critically ill COVID-19 patients [11, 12]. Therefore, early diagnosis of COVID-19 patients also suffering from shock may prove effective in early ICU follow-up and intubation decisions. There are some markers used to detect early shock, such as qSOFA, SI, MSI, and NLR values.
After the new definition of sepsis [7] was published, the qSOFA score was recommended for pre-evaluation in intensive care admissions with a diagnosis of septic shock [13]. We also found that qSOFA is a practical and useful indicator of COVID-19-related ICU mortality in emergency patient evaluation.
Another sepsis marker is NLR. Previous studies have shown that NLR during hospitalization was an independent predictor of in-hospital mortality in COVID-19 patients with sepsis who were admitted to the emergency service. In a retrospective analysis of 63 patients in China, NLR was found to be an independent risk factor for severe COVID-19 [14]. In a meta-analysis involving 1579 patients, NLR was found to be an acceptable predictor of disease severity and mortality in COVID 19 patients. It is stated that it can contribute to reducing the overall mortality rate of COVID 19 by helping clinicians to detect serious cases early, triage them quickly, and start their treatment effectively [8]. In this review, NLR> 9.11 has been associated with mortality in critically ill patients. In our study, we found that NLR is significantly higher in the mortality group, but is not an independent risk factor.
It has been reported that SI is a useful parameter for early diagnosis of sepsis, acute critical illness, unplanned ICU transfers, risk stratification for pulmonary embolism, acute

myocardial infarction, and death [5, 15, 16]. Besides, the conducted studies have indicated that high shock index values are associated with death from critical illnesses [17]. In addition to similar benefits, mean blood pressure values are taken into account in MSI, and guidelines recommend the initiation and titration of vasopressor treatments based on MAP. The Surviving Sepsis Campaign guidelines on the management of adults with COVID-19 in the ICU are based on MAP monitoring, not vital signs such as SBP, to guide both fluid and vasoactive requirements [18]. Additionally, Nathan J. et al. [6] showed that there is a significant risk of death in critically ill patients with high MSI within the first 24 hours after admission to the ICU. Considering that MSI can be easily calculated at the bedside, it is stated that its use in practice may be beneficial for clinicians to initiate interventions earlier that may increase survival.

Based on the fact that COVID-19 is a newly-recognized disease and progresses in combination with shock in critically ill patients, we retrospectively evaluated SI and MSI to determine the ICU follow-up indication, and found that they could not predict ICU mortality. There are also studies in the literature using similar markers to predict the need for early diagnosis of intubation in septic shock. Most COVID-19 patients with severe respiratory failure should be followed up in the ICU due to the need for intubation and IMV. However, while making this decision, it is necessary to consider a number of factors, including timing. There are also views opposing the idea that early intubation may be beneficial [19-22].

In the study by Sangita Trivedi et al. [23], pre-intubation SI and MSI were addressed as easily accessible, non-invasive, bedside clinical tools to identify patients with high complication risk. While a pre-intubation SI value of ≥ 0.90 was defined as an important predictor of post-intubation hypotension and ICU mortality, MSI was stated to be useless in predicting any outcome. Although deciding on the necessity of tracheal intubation in COVID-19 intensive care follow-up is of significance in terms of survival, we could not find any significant contribution of qSOFA, MSI, SI or NLR values in predicting intubation.

Conclusion

In this study, we found out that no scoring system can predict the requirement of intubation, but qSOFA is effective in showing mortality when making ICU follow-up decisions in COVID-19 patients consulted in the emergency department. We concluded that we still need parameters and studies in larger series that will guide us in making this critical decision.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None*

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Sharma A, Tiwari S, Deb MK, Marty JL. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies. Int J Antimicrob Agents. 2020;56(2):106054.

2. Wu Z, Mc Googan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13): 1239-42.

3. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV out break originating in Wuhan, China: a modeling study. Lancet. 2020;395(10225):689–97.

4. Çiyiltepe F, Saraçoğlu A, Bilir Y, Deniz EA, Bombacı E, Saraçoğlu KT. The role of IL-6 receptor inhibitor treatment in critical patient monitoring with COVID-19. Signa Vitae. 2021. 17(3);174-80.

5. Keller AS, Kirkland LL, Rajasekaran SY, Cha S, Rady MY, Huddleston JM. Unplanned transfers to the intensive care unit: the role of the shock index. J HospMed. 2010;5(8):460-5.

6. Smischney NJ, Seisa MO, Heise KJ, Schroeder DR, Weister TJ, Diedrich DA. Elevated Modified Shock Index Within 24 Hours of ICU Admission Is an Early Indicator of Mortality in the Critically Ill. J Intensive Care Med. 2018;33(10):582-8.

7. Singer M, Deutschman CS, Seymour CW, Shankar-HariM, Annane D, Bauer M, et al. The third international consensus definition for sepsis and septic shock (sepsis-3). JAMA. 2016;315(8):801-10.

8. Li X, Liu C, Mao Z, Xiao M, Wang L, Qi S, et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. CritCare. 2020;24(1):647.

9. Grasselli G, Greco M, ZanellaA, Albano G, Antonelli M, Bellani G, et al. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. JAMA Intern Med. 2020;180(10):1345-55.

10. Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. Lancet. 2020;395(10235):1517-20.

11. Zhou F, Yu T, Du R. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62.

12. Hantoushzadeh S, Norooznezhad AH. PossibleCause of Inflammatory Storm and Septic Shock in Patients Diagnosed with (COVID-19). Arch Med Res. 2020;51(4):347-8.

13. Finkelsztein EJ, Jones DS, Ma KC, Pabón MA, Delgado T, Nakahira K, et al. Comparison of qSOFA and SIRS for predicting adverse outcomes of patients with suspicion of sepsis outside the intensive care unit. Crit Care. 2017;21(1):73.

14. Xia X, Wen M, Zhan S, He J, Chen W. An increased neutrophil/lymphocyte ratio is an early warning signal of severe COVID-19. Nan Fang Yi Ke Da Xue Xue Bao. 2020;40(3):333-6.

15. Berger T, Green J, Horeczko T, Hagar Y, Garg N, Suarez A, et al. Shock index and early recognition of sepsis in the emergency department: a pilot study. West J Emerg Med. 2013;14(2):168-74.

16. Toosi MS, Merlino JD, Leeper KV. Prognostic value of the shock index along with transthoracic echocardiography in risk stratification of patients with acute pulmonary embolism. Am J Cardiol. 2008;101(5):700-5.

17. Sloan EP, Koenigsberg M, Clark JM, Weir WB, Philbin N. Shock index and prediction of traumatic hemorrhagic shock 28-day mortality: data from the DCLHb resuscitation clinical trials. West J Emerg Med. 2014;15(7):795-802.

18. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854-87.

19. Tobin MJ. Principles and practice of mechanical ventilation. 3rd ed. New York: Mc Graw-Hill; 2013.

20. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med. 2013;369(22):2126-36.

21. Marini JJ, Gattinoni L. Management of COVID-19 respiratorydistress. Jama. 2020;323(22):2329-30.

22. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 2020;46(6):1099-102

23. Trivedi S, Demirci O, Arteaga G, Kashyap R, Smischney NJ. Evaluation of preintubation shock index and modified shock index as predictors of postintubation hypotension and other short-term outcomes. J CritCare. 2015;30(4):861.

How to cite this article:

Fulya Çiyiltepe, Ayten Saraçoğlu, Özge Yıldız, Yeliz Bilir, Elif Bombacı, Kemal Tolga Saraçoğlu. Are shock index, modified shock index, NLR and qSOFA useful in making COVID-19 intensive care follow-up decisions? Ann Clin Anal Med 2021;12(12):1423-1426